UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/642,609	08/17/2000	Yoshinari Kumagai	BEAR-004	6929

24353 7590 04/18/2003

BOZICEVIC, FIELD & FRANCIS LLP
200 MIDDLEFIELD RD
SUITE 200
MENLO PARK, CA 94025

EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/642,609	KUMAGAI ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-11 and 17-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

ACKNOWLEDGMENT OF SEQUENCE LISTING, IDS, RESPONSE TO THE RESTRICTION REQUIREMENT AND STATUS OF THE CLAIMS

1. The sequence listing requirement filed 8/29/00, the Information Disclosure Statement (IDS) and Form PTO-1449 filed 11/28/00 and 2/19/02, respectively and the response to the restriction requirement filed 2/10/03 are acknowledged, entered and considered. Claims 1-19 are now pending in the application.

ELECTION WITH TRAVERSE

2. Applicant's election with traverse of Group II (claims 12-16) in Paper No. 11 is acknowledged. The traversal is on the ground(s) that there would be no significant burden on the Examiner if all the claims (i.e., claims 1-19) are examined in the present application because the search and examination of the entire application can be made without serious burden as stated in M.P.E.P. § 803. The argument is not persuasive because Groups I-V are classified in various classes and subclasses and have different products and method of use.

Further, Inventions I and II-V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, methods II-V are alternative methods of use of the peptidic compound and composition thereof of Group I (claims 1-11) as claimed can be used in a

materially different process such as in a method of treating hyper phosphatemia, or in a method of increasing incorporation of phosphorus into bone, or in a method of increasing bone strength or in a method of treating a bone disease as claimed in Groups II-V, respectively.

Furthermore, Inventions II-V, are related as independent methods which are not connected in design, operation or effect. Although, the methods of Groups II-V use the same composition, however, the methods have different functions and different effects. The groups require different patent and literature search and a reference teaching a method of increasing incorporation of phosphorus into bone will not teach a method of increasing bone strength nor a method of treating a bone disease and *vice versa*. Thus, the methods of Groups II-V as grouped are independent and distinct inventions which differ in material make up and composition requiring different reaction conditions. Hence, practice of one invention does not require the other for ultimate use and as such is capable of separate manufacture, use and sale.

With respect to compositions of Groups I and II-V, the composition of Group I comprises a peptide compound having monomer units selected from the group consisting of a coded amino acid, a non-coded amino acid, and a synthetic amino acid of the general structural formula as recited in claim 2 while the compositions of Groups II-V comprises a peptide compound having 4 to 30 residues which are not defined. Thus, the compositions have different structures, functions and different effects. Hence, one does not require the other for ultimate use and as such is capable of separate manufacture, use and sale, and is novel and patentable over each other.

Therefore, claims 1-11 and 17-19 (Groups I and III-V) are withdrawn as non-elected invention in view of the reasons discussed above; hence, the Office action is directed to the merits of claims 12-16 as *per* elected invention.

The requirement is still deemed proper and is therefore made FINAL.

OBJECTION TO THE ABSTRACT

3. The disclosure of the abstract is objected because it contains a file locator "F:\DOCUMENT\BEAR(formerly 8302)\004\BEAR-004appln.wpd". Deletion of the file locator from the disclosure of the abstract would obviate this objection.

OBJECTIONS TO TRADEMARKS AND THEIR USE

4. The use of the trademark "(Crl:CD®IGS BR)" has been noted in this application. This trade mark has not been capitalized, it should be capitalized whenever it appears and be accompanied by the generic terminology. Although, the use of trademark is permissible in patent applications, the proprietary nature of the mark should be respected and every effort made to prevent its use in a manner which might adversely affect its validity as trademarks.

Further, the specification which specifies the generic terminology should include published product information sufficient to show that the generic terminology or the generic description is inherent in the article referred by the trademark. These description requirement are made because the nature and composition of articles denoted by trademark can change and affect the adequacy of the disclosure.

CLAIMS REJECTION-35 U.S.C. § 112 2nd PARAGRAPH

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12 and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is indefinite in the recitation "....4-30 residues.....having at least one residue....." because it is not clear what kind of residues and/or residue the claim is referring to. If the claim is referring to amino acid residues or residue, then, amendment of the claim to recite ".....4-30 amino acid residues.....having at least one amino acid residue....." would obviate this rejection.

CLAIM REJECTIONS-35 U.S.C. § 103(a)

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reynolds (U.S. Patent No. 5,015,628) in view of Monier-Faugere et al., (Cecil Textbook of Medicine, 21st Edition, Volume 2, Chapter 266, pages 1409-1414, edited by Goldman, Published by W.B. Saunders Company, 2000).

Independent claim 12 is directed to the use of a compound which is defined as a compound characterized by a) oral bioavailability, b) 4-30 residues, and c) having at least one residue which is phosphorylated or which is phosphorylatable *in vivo* or *in vitro*. The prior art of Reynolds renders the claim obvious because it teaches a composition comprising a phosphopeptide having from 5-30 amino acids, wherein the composition is in a form of pharmaceutical composition and administered orally to a mammal in a therapeutically effective amount (See e.g., col. 1, lines 10 to col. 2, lines 8 and col. 3, lines 9-14). The reference of Reynolds on col. 2, lines 50-68 further teaches that the composition preferably comprises a peptide which is present as 0.01 to 10% by weight which is a unit of 1 to 1000, and as such is

equivalent to a composition comprising 1 to 1,000 mg of the peptide compound as claimed in claim 13 (i.e., since mg reflects weight unit). Also, the reference discloses that the peptidic compound exhibits a reduction in hydroxyapatite dissolution rate of at least 15% which meets the limitation of reduction serum phosphate levels 5% or more of claim 15 because on col. 6, lines 59-61, the reference states that the reduction in hydroxyapatite dissolution was related to phosphoserine content and spacing within a peptide.

The references of Reynolds differs from claims 12-16 in not teaching a method of treating hyperphosphatemia (an excess amount of phosphate in the blood) by administering orally the peptidic compound claimed and the duration time of the administration. However, the primary reference of Reynolds on col. 8, lines 27-34 states that the ability of these peptides to sequester calcium phosphate can be utilized in the treatment of various rarefying bone diseases. These peptides can significantly increase the absorption of calcium, phosphate and iron in the gut. Hence, pharmaceutical vehicles (e.g., enteric capsules) or foods containing calcium phosphate T1 and ferrous phosphate T1 can be used for the treatment of osteoporosis/osteomalacia and anemia. For support, See the secondary reference of Monier-Faugere et al., (Cecil Textbook of Medicine, 21st Edition, Volume 2, Chapter 266, pages 1409-1414, edited by Goldman, Published by W.B. Saunders Company, 2000) which teaches the association of diseases of bone and bone mineral metabolism. For example, on page 1409, the reference teaches the relationship and/or coexistence of calcium, parathyroid hormone (PTH) and phosphate in renal osteodystrophy which encompasses a wide variety of derangements in mineral and bone metabolism. Further, on

page 1410, the reference discloses the associations and mechanisms of how hyperphosphatemia result in advanced renal failure in which the increased serum phosphorus levels and PTH further decreases serum calcium through physicochemical binding affecting the histologic pattern of renal osteodystrophy resulting in a profound decrease in bone turnover, i.e., low number of active remodeling sites resulting in bone resorption and suppressed bone formation.

Furthermore, the primary reference of Reynolds suggests the treatment of various rarefying bone diseases such as osteoporosis/osteomalacia (i.e., any diseases/conditions associated with increase of phosphate). Thus, in view of this and in view of the secondary reference, one of ordinary skill in the art would understand that the phrase "treatment of various rarefying bone diseases" would include treatment of hyperphosphatemia. Therefore, given the combined teachings of the prior art, one of ordinary skill in the art would be motivated to administer orally the peptidic compound of the primary reference for the intended purpose of treating conditions associated with elevated phosphate levels (i.e., hyperphosphatemia).

With respect to repeatedly administering the peptidic composition once a day or more over a period of 30 days or more (claim 16); the reference states that the composition is administered for a prolonged period of time, wherein the prolonged period of time may be short as one day but is more preferably a period of weeks (> 7 days) or months (> 30 days) (See e.g., col. 3, lines 35-48). Thus, in view of this, one of ordinary skill in the art would understand that the duration of the administration time depends on the condition of the individual. Hence, the duration of the administration time, dosage levels and route of administration varies depending

on a number of factors including the nature of the subject to be treated (age, sex, weight, etc.), the particular nature of the condition to be treated and its severity, the particular compound used as active ingredients, the route of administration, the formulation, and the judgment of the practitioner.

Therefore, in view of the above and in view of the combined teachings of the prior art, one of ordinary skill in the art would have been motivated at the time the invention was made to employ a method of treating hyperphosphatemia by administering orally to an individual a therapeutically effective amount of a composition comprising a peptidic compound characterized by a) oral bioavailability, b) 4-30 residues, and c) having at least one residue which is phosphorylated or which is phosphorylatable *in vivo* or *in vitro*, and repeatedly administering the composition over a period of time, thereby reducing serum phosphate levels in the individual, absent of sufficient objective factual evidence or unexpected results to the contrary.

CITATION OF RELEVANT PRIOR ART

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kumagai et al., in (U.S. Patent No. 6,306,822 and WO 98/00156) teach use of phosphopeptides for treating bone diseases. The cited pertinent art are from the same inventors and it is not art under 35 U.S.C. 102.

CONCLUSION AND FUTURE CORRESPONDENCE

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The appropriate fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Christopher S. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Mohamed/AAM

April 11, 2003